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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,830	01/08/2001	Sydney Brenner	5525-0046.30	6856

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PERKINS COIE LLP
P.O. BOX 2168
MENLO PARK, CA 94026

EXAMINER	
SISSON, BRADLEY L	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 09/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/756,830	BRENNER ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7,15 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 25 July 2005 has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-4, 6, and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. In claim 1, step (a), one is to provide an "amplicon," which is to comprise "one or more words," wherein each "word" is to comprise "an oligonucleotide having a length of from three to fourteen nucleotides." In accordance with step (b), one is to clave the "amplicon," and thereby produce "a first opened amplicon" (emphasis supplied).

5. Page 6 of the specification provides the following definition of said term.

> As used herein, "amplicon" means the product of an amplification reaction. That is, it is a population of polynucleotides, usually double stranded, that are replicated from a few starting sequences. Preferably, amplicons are produced either in a polymerase chain reaction (PCR) or by replication in a cloning vector.

6. As seen above, the amplicon is preferably that produced by PCR, which would yield linear DNA. Accordingly, it is not clear how cleaving linear DNA would cause one to produce anything but more linear DNA. Additionally, it is less than clear how, when there is a plurality of words in the starting material, and that there is only one word in the resulting fragment. And it is equally unclear as to how one would produce but a single fragment when one cleaves the linear nucleic acid. Seemingly, there would be at least two fragments generated, and possibly more when the amplicon comprises more than one recognition site for a restriction endonuclease.

7. Claim 1 is confusing where in step (a) is stated "providing a repertoire of same-length oligonucleotide tags" and then later stating "a duplex consisting of a word of the set and the complement of any other word of the set." An oligonucleotide is construed as being single stranded. A duplex structure could comprise the "word" and its complement. It is not clear how an "oligonucleotide" (single stranded) and "a duplex" (double stranded) both consist of a word.

8. Claims 2-4, 6, and 7, which depend from claim 1, fail to overcome this issue and are similarly rejected.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-4, 6, 7, and 15-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains,

or with which it is most nearly connected, to make and/or use the invention. The claims are directed to a) a method of synthesizing a repertoire of oligonucleotide tags, and b) a repertoire of said tags.

11. Aside from teaching how to make the invention, the specification must also enable the use of the product so produced (and claimed). Said disclosure must also disclose the best mode contemplated by applicant for both the claimed method and the claimed product.

12. The specification provides the following examples:

a. Example 1, "Repertoire Synthesis by Repeated Cycles of Cleavage, Self-Selection, Ligation, and Amplification," pages 14-16;

b. Example 2, "Repertoire Synthesis by Convergent Assembly of Error-free Oligonucleotide Tag Precursors," pages 16-18;

c. Example 3, "Construction of an Eight-Word Tag Library," pages 18-24.

Clearly, the three examples do not each the skilled artisan how to recognize useful over non-useful oligonucleotides or vectors.

13. Assuming *arguendo*, that one of skill in the art could make a repertoire of oligonucleotide tags, the specification does not teach how one would be able to synthesize only useful oligonucleotide tags. Furthermore, the specification does not teach a reproducible and useful procedure whereby aid useful tags are recognized and used. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200,

> 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
>
> *****
>
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. <u>However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art.</u> It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (Emphasis added)

Accordingly, and in the absence of convincing evidence to the contrary, 1-4, 6, 7, and 15-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

14. Claims 1-4, 6, 7, 15, and 16 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

15. In order to satisfy the utility requirement, either the resultant product has utility or that the product's utility is derived downstream in its use in a method, which is recognized as satisfying the utility requirement.

16. Claims 1-4, 6, and 7 are all drawn to a method of synthesizing a repertoire of oligonucleotide tags. Claims 15 and 16 are drawn to said set of oligonucleotide tags. The specification has not been found to set forth a specific and substantial utility for the product and a review of the disclosure fails to find where the resultant and clamed product, when used, would in turn meet the utility requirements. Specifically, it is not enough that one can synthesize, or claim outright, a "tag" that could be used to determine if a complementary sequence is present, e.g., an expressed sequence tag or EST, a sequence for which no known utility exists. While the tags can be used to determine if a complementary sequence exists, all nucleic acids can be used in such a manner. While one may elect for that which exhibits less cross-hybridization, the intended target, even if unique, must have a specific and substantial utility. Simply determining its existence does not suffice.

17. The situation at hand is analogous to that of *In re Fisher* (CAFC, 04-1465, decided 07 September 2005). In *Fisher* the disclosure provided five ESTs and assertions as to their potential utility. Here, applicant is claiming a method of producing "tags" and the "tags" per se. Like *Fisher*, no evidence has been presented that the product of the claimed method or the product outright, does in fact have any of the alleged utilities. Further, the aspect of finding complementary sequences (which could be an EST) is not considered to be a substantial utility as the utility requirement is not satisfied for like the ESTs of *Fisher*, the product, even it had been produced/found, would be at best the subject of further research and development so to

determine if it does in fact have any real value. In view of the clear need for the product of the claimed invention to have utility, and no convincing showing has been made in this regard as to its satisfaction, no specific, substantial, and credible utility exists in readily available form a the time of filing.

18. Claims 1-4, 6, 7, 15 and 16 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 102

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by GIBCO BRL Products & Reference Guide (GIBCO).

21. For purposes of examination the "repertoire of oligonucleotides" need only comprise two oligonucleotides (though many more could be present) and that they can range in length "from three to fourteen nucleotides."

22. GIBCO, page 17-19, discloses random primers for sale. Said primers are described as comprising all possible hexanucleotides. By default, the random primes would comprise the now claimed oligonucleotides.

Conclusion

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

24. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

25. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
16 September 2005